

Plasma renin activity in coarctation of aorta before and after surgery

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Plasma renin activity was measured in 11 cases of coarctation of the aorta before and after operation. The values of plasma renin activity in the recumbent position before operation were significantly lower than in the control group. After surgery plasma renin activity rose to normal levels. There was no correlation between plasma renin activity levels and arterial blood pressure. The renin-angiotensin system seems not to be involved directly in the maintenance of hypertension in patients with aortic coarctation.

The pathogenesis of the arterial hypertension in the upper part of the body in cases of coarctation of the aorta is not clear. Patients with coarctation are necessarily studied when compensatory changes in the circulation have already occurred, as shown by the similar values of renal blood flow in these patients when compared with normal subjects (Werko *et al.*, 1956; Culbertson *et al.*, 1957; Kirkendall, Culbertson, and Eckstein, 1959; Timmis and Gordon, 1964; Kroetz, Kirkendall, and Kioschos, 1968). In attempts to study the mechanism(s) initiating hypertension, most workers have relied on observations made during the first hours or days after experimental constriction of the aorta. More recently, long-term experiments have been reported (Yagi *et al.*, 1968; Ledingham, 1971) on a model more similar to the conditions encountered in man. The latter studies suggest that the chronic phase of hypertension with coarctation of the aorta is not associated with an increase in peripheral plasma renin activity.

Observations in patients with coarctation before and after surgical restoration of normal haemodynamics have been performed only rarely. Such studies are important because after successful operation the mean arterial blood pressure as well as the pulsatility of blood flow is increased in the area distal to the narrowed aorta.

The aim of this study was to measure the plasma renin activity in patients with coarctation of the aorta before and after successful surgical treatment in order to assess the possible role of the renin-angiotensin system in the production of the hypertension in these patients.

Subjects and methods

The study group consisted of 11 patients aged 5 to 20 years (mean 10.3 years). The diagnosis of coarctation of the aorta was established on the basis of the usual clinical criteria and confirmed at operation in each case. In 4 patients there was also a persistent ductus arteriosus (Cases 4, 7, 9, and 11), while another (Case 5) had clinical evidence of aortic regurgitation. All the examinations were done first before the operation, repeated 2 to 4 weeks after operation, and again 3 to 6 months after operation. No drugs were given during this period.

Plasma renin activity was assayed in blood taken from an antecubital vein after at least 5 hours in the recumbent position in patients taking a diet containing 80 to 110 mmol sodium daily ('recumbent plasma renin activity'). During the next 24 hours the patients received a sodium-restricted diet (less than 10 mmol Na/day) and 40 to 80 mg frusemide in two divided doses orally. The next day blood samples were taken again, after the patient had maintained the upright position, walking or standing, for 2 hours ('upright plasma renin activity'). Plasma renin activity was assayed by the method described by Boucher *et al.* (1964) and was expressed in terms of nanograms of angiotensin II released under the influence of the enzyme per 100 ml of plasma during incubation for 3 hours at 37°C.

Immediately after sampling the blood for 'recumbent plasma renin activity', arterial blood pressure was measured in the upper and lower extremities on the left side (auscultatory method of Korotkoff). Within the next 24 hours, sphygmo-oscillometry was performed in each case on the same extremity (using an Infraton OS 3 sphygmo-oscillograph, Boucke-Brecht type, with synchronized automatic recording of blood pressure in mmHg). Two curves were recorded; the first was taken during uniformly falling pressure in the cuff (from 300 to 0 mmHg (40 to 0 kPa)) and the mean blood pressure

TABLE I Vascular and renal function tests

		No. of patients	Before operation		After operation		t	P
			Mean	Range	Mean	Range		
Time of ascending pulse wave (s)		11	0.25	0.20-0.36	0.18	0.14-0.30	5.22	< 0.001
Pulsatile volume (mm ³)	Left upper extremity	11	207	68-662	121	50-346	3.17	< 0.01
	Left lower extremity	11	116	16-210	241	138-312	-7.21	< 0.001
Clearance PAH (ml/min per 1.73 m ²)		10*	395	248-587	391	142-699	0.08	NS
Renal blood flow (ml/min per 1.73m ²)		10*	635	386-1029	651	233-1092	-0.19	NS
Radioisotope renography (s)	Vascular and tubular phase	8†	297	150-480	278	180-367	0.44	NS
	Excretory phase	8†	426	240-615	348	135-488	1.50	NS

* Excluding Case 11.

† Excluding Cases 2, 9, and 10.

was determined from the highest pulse amplitude; the second tracing was recorded at constant pressure equal to the mean arterial pressure. The time of the ascending pulse wave in the lower extremity (in seconds) and pulsatile blood volume of the extremity (in mm³) were calculated from this curve as compared with the standard pattern (Singer and Kudybyn, 1969).

Serum creatinine concentration, para-aminohippuric acid clearance (Kokot, 1969) and ¹³¹I-labelled sodium hippurate renography was performed in 8 patients (Table 1). Renal blood flow was calculated from the estimated renal plasma flow and the haematocrit.

Plasma renin activity was also determined in 10 normal children aged 6 to 14 years (mean 10.3 years) under

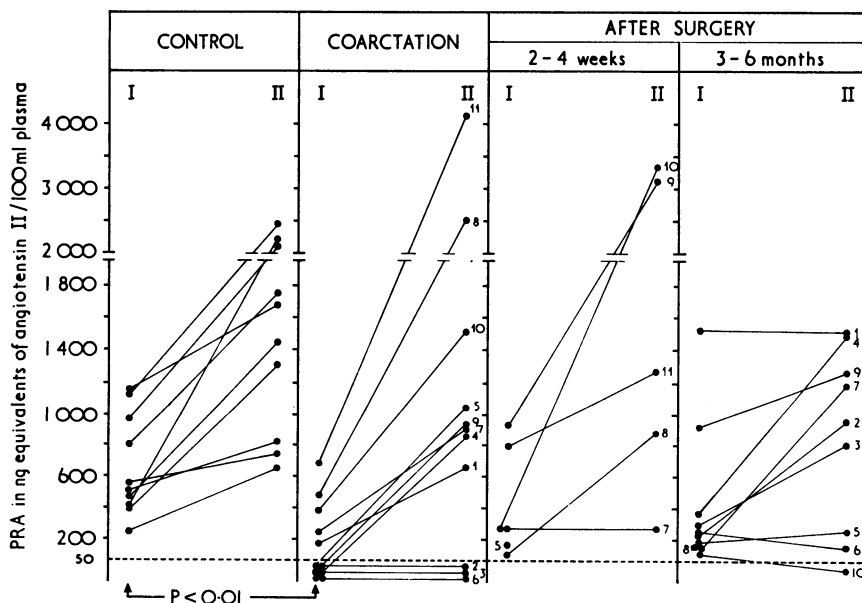


FIG. Plasma renin activity in recumbent (I) and upright (II) positions.

TABLE 2 Blood pressure and plasma renin activity

Case No.	Age (yr) sex	Sampling	Blood pressure (mmHg)*		Mean blood pressure (mmHg)		Plasma renin activity (ng/100 ml)	
			Arm	Leg	Arm	Leg	Recumbent	Upright
1	6, M	Before	120/70	†	100	90	180	660
		After 4 mth	105/60	115/80	90	90	1575	1500
2	6, F	Before	160/90	†	110	85	< 50	< 50
		After 5 mth	120/70	110/70	105	105	220	945
3	7, M	Before	155/60	†	100	70	< 50	< 50
		After 4 mth	115/70	115/80	90	90	300	807
4	14, M	Before	140/80	†	110	90	< 50	887
		After 3 mth	120/70	135/70	100	115	375	1590
5	11, M	Before	140/95	†	130	100	< 50	1027
		After 4 wk	ND	ND	ND	ND	150	ND
		After 6 mth	120/80	125/80	100	110	195	247
6	20, M	Before	220/80	†	130	90	< 50	< 50
		After 3 mth	170/70	120/70	110	100	225	140
7	9, M	Before	130/70	†	100	85	262	900
		After 17 dy	95/65	90/60	100	95	270	270
		After 5½ mth	95/65	100/60	90	100	123	1163
8	11, F	Before	175/80	†	110	85	495	2494
		After 3 wk	160/75	Trace	90	115	110	850
		After 5½ mth	180/80	Trace	100	100	187	ND
9	8, F	Before	130/70	†	120	90	< 50	900
		After 4 wk	115/70	120/80	90	95	922	3000
		After 6 mth	115/60	115/70	95	100	915	1245
10	16, M	Before	160/80	†	140	100	397	1575
		After 2 wk	160/80	Trace	100	115	270	3300
		After 6 mth	150/85	Trace	115	105	123	< 50
11	5, M	Before	130/80	†	110	75	690	4200
		After 2 wk	110/80	90/60	100	90	794	1250

* Conversion from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

† No value obtainable.

ND = not determined.

the same dietary circumstances. The results were analysed by the paired 't' test (Table 1) and group 't' test (Fig.).

Results

After operation femoral pulses were palpable in each case. The time delay of the ascending pulse wave in the legs shortened significantly in all cases after operation (Table 1). The pulsatile volume also changed significantly becoming less in the upper extremity, and increasing in the lower limb.

As shown in Table 1, renal haemodynamics did not change after operation; the serum creatinine level also remained unaltered (less than 106 μ mol/l (1.2 mg/100 ml) in each case).

Arterial blood pressure in the upper extremities decreased after operation in 9 of the 11 patients (Table 2), while the blood pressure in the lower limbs usually increased (average change 15 mmHg (2 kPa)). In two patients (Cases 8 and 10), arterial blood pressure in the lower extremities was still

unmeasurable, though the femoral pulses became weakly palpable and the mean blood pressure as well as pulsatile volume increased.

The plasma renin activity in the control group of 10 children while recumbent was 667 ± 315 ng/100 ml of angiotensin II rising to 1493 ± 611 ng/100 ml in the upright position (Fig). These values are higher than those for healthy adults determined in our laboratory: 219 ± 24 ng/100 ml recumbent and 1082 ± 100 ng/100 ml in the upright position (Kokot and Kuska, 1972).

Table 2 and the Fig show the plasma renin activity estimations. In 6 patients while recumbent before operation, only trace values of plasma renin activity were found: in 2 others the levels were sub-normal and plasma renin activity was normal in the remaining 3 cases. Recumbent plasma renin activity in cases of coarctation of the aorta was significantly lower than in the control group ($P < 0.01$). After operation, plasma renin activity increased in 8 patients and the mean value was no

TABLE 3 Plasma renin activity before (A) and after surgery (B), as determined by various authors

Author	Position	No. of patients	A			No. of patients	B		
			Low	Normal	High		Decrease	No change	Increase
Brown <i>et al.</i> (1965)	Recumbent	4		4		1			1
Genest <i>et al.</i> (1965)	Recumbent	4		2	2				
Pickens (1967)	Recumbent	1			1	1	1		
Imbs, Desaulles, and Bloch (1968)	Recumbent	6	1	2	3				
	Upright	4	1	2	1				
Kroetz <i>et al.</i> (1968)	Recumbent	5		5					
Amsterdam <i>et al.</i> (1969)	Recumbent	16	15†		1				
Werning <i>et al.</i> (1969)	Recumbent	10		9	1				
	Upright	10		9	1				
Strong <i>et al.</i> (1970)	Recumbent	12	1	7	4	12‡	6	4	2
	Upright	3		3					
Present paper	Recumbent	11	6	5		11	2		9
	Upright	11	3	6	2	11	4	2	5
Totals	Recumbent	69	23	34	12	25	9	4	12
	Upright	28	4	20	4	11	4	2	5

† All values below the mean control value.

‡ Only long-term (mean 112 days) postoperative data.

longer significantly different from the control group.

Before surgery 'upright' plasma renin activity was subnormal in 3 patients, abnormally high in 2 patients, and within the normal range in the remainder. The influence of surgical repair on upright plasma renin activity was variable (Fig.).

Discussion

Surgery was successful in returning palpable femoral pulses in all the patients; blood pressures could be measured in the lower extremities after operation in all but 2 patients and the mean blood pressure rose significantly in 10 of the 11 cases.

The significant increase in pulsatile volume and the conspicuous shortening of the ascending arm of the pulse wave in the lower extremities after operation are taken as indirect evidence of increasing pulsatility of blood flow in the whole area below the previously narrowed aorta. Renal blood flow, measured before and after operation, was normal. Thus, the renal haemodynamics in the patients appeared independent either of the aortic lesion or of changing systemic circulation.

From the observations on plasma renin activity it appears that hypertension in aortic coarctation is not associated with raised values. Indeed in half the patients only trace levels of plasma renin activity were noted with the patients recumbent. The increase in plasma renin activity provoked by sodium depletion and the upright posture raised the levels to the normal range in 8 cases while no change was detected in the remainder.

After operation, recumbent plasma renin activity increased in the majority of patients, including those with trace levels before operation. No correlation was found between plasma renin activity and arterial blood pressure.

Previous measurements of the renin-angiotensin system in patients with coarctation yielded variable results. Some authors determined angiotensin II levels in the blood; Morris, Robinson, and Scheele (1964) found raised levels in all 9 patients, but their results were methodologically questionable (Werning *et al.*, 1969). Massani *et al.* (1966) in 2 patients and Ueda, Kaneko, and Takeda (1966) noted normal blood values of angiotensin II. Sealy (1967) examined 5 patients and found normal angiotensin levels in 3 while high values were reported in the other 2 cases, both of whom had complications. Timmis and Gordon (1964) examined 3 patients and found no significant changes in excretion of aldosterone in 24-hour urine either before or after operation.

Plasma renin values have been studied more frequently in this syndrome. The results obtained by various authors are given in Table 3. It can be seen that of a total of 69 cases the levels were normal in 34 (50%), while in the other cases the levels were either higher (12) or lower (23) than the normal range. Similar results were obtained with plasma renin activity in upright position; 85.7 per cent of cases had low or normal values. The evaluation of the role and the significance of the renin-angiotensin system in coarctation of the aorta is difficult, since

the mechanisms controlling the autoregulation of renal blood flow and of renin release are still not clear.

In a recently published review on the physiological significance of renin, Stein and Ferris (1973) mention 10 factors with a possible influence on the secretion of this enzyme. Two of them seem more important: arterial blood pressure (baroreceptor theory formulated by Tobian (1967)) and the sodium macula densa theory, according to Vander and Miller (1964).

As far as we are aware the only other report including both pre- and postoperative measurements of renin in coarctation is that of Strong *et al.* (1970). They did not find a rise in recumbent plasma renin activity after operation, as was observed in our series.

In view of these collected results, it seems evident that coarctation of the aorta in subjects older than 5 years is not usually associated with a decrease in renal blood flow nor in renal function. Neither does it provoke a persistent increase in plasma renin levels; on the contrary circulating renin is normal or low. After surgical repair of the aortic lesion plasma renin activity seems to enter the normal range. Thus, the mechanisms of prolonged systemic hypertension in aortic coarctation seem not to be related directly to overactivity of the renin-angiotensin system.

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